*THIS OPINION WAS NOT WRITTEN FOR PUBLICATION*

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 44

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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*Ex parte* ROBERT J. MELLO
WILLIAM P. TEW
and NARLIN B. BEATY

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Appeal No. 95-2655
Application 07/912,029[1]

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ON BRIEF

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Before SCHAFER, *Vice Chief Administrative Patent* Judge, and JOHN D. SMITH and WALTZ, *Administrative Patent Judges*.

WALTZ, *Administrative Patent Judge*.

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[1] Application for patent filed July 9, 1992. According to appellants, this application is a continuation of Application 07/798,835, filed November 25, 1991, now abandoned, which is a continuation of Application 07/542,389, filed June 23, 1990, now abandoned, which is a continuation-in-part of Application 07/384,530, filed July 24, 1989, now abandoned.

*DECISION ON APPEAL*

This is an appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 to 20, which are all the claims in this application[2].

According to appellants, the present invention is directed to physiological visco-elastic formulations which contain hyaluronates in a balanced salt solution including calcium and magnesium ions. One important feature of these formulations is that they resemble or approach the composition of the aqueous humor of the human eye. These compositions have enhanced ocular compatability and are useful in intraocular surgical procedures (brief, pages 1-2).

Appellants' brief includes a statement that the claims on appeal do not stand or fall together (page 2). Contrary to the examiner's assertion on page 2 of the answer, appellants

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[2] The final rejection, mailed March 24, 1993, states that claims 1 to **22** are pending and are rejected (see PTOL-326, Part II, Items 1 and 4, and page 3, line 2, of the Final Rejection). However, page 2 of the Final Rejection correctly states that claims 1 to 20 are presented for examination and are "again rejected". Since appellants' brief states that claims 1 to 20 are pending and have been finally rejected (page 1), the examiner's error in the Final Rejection is harmless.

do present reasons in support of this statement (see pages 12-13 of the brief). However, these reasons advanced by appellants are merely statements setting forth the limitations of the dependent claims and do not provide reasons why these claims are patentable over the reference. Therefore, the claims stand or fall together. See 37 CFR § 1.192 (c)(5)(1993) and *In re Herbert*, 461 F.2d 1390, 1391, 174 USPQ 259, 260 (CCPA 1972)("While appellant's reply brief emphasized that his claims 'are of varying scope and do not stand or fall together,' he has failed to point out what relevance the additional limitations have to the patentability of the narrower claims...").

The subject matter on appeal is adequately illustrated by claim 1, reproduced below:

1. A physiological visco-elastic formulation comprising hyaluronate salt in an amount in the range of about 0.1% to about 5% by weight in a balanced salt solution containing calcium ions present in a concentration in the range of about 2.6 mM to about 3.9 mM and magnesium ions present in a concentration in the range of about 1.2 mM to about 1.8 mM, said formulation being ionically and osmotically balanced and being free of phosphates.

The reference relied upon by the examiner is:

Derwent Abstract # C87-081037[3], published March 6, 1987 (hereafter the "Abstract"), an abstract of Yamamoto et al. (Yamamoto), Japanese 62-122671, Laid Open June 3, 1987.

Claims 1 to 20 stand rejected under 35 U.S.C. § 103 as unpatentable over the Abstract[4]. We *affirm* this rejection but, for reasons noted below, we denominate this "affirmance" as a new ground of rejection pursuant to our authority under 37 CFR § 1.196(b).

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[3] The examiner lists the abstract number as "C87-08/037" (answer, page 2), but from the copy of record it appears the abstract number is "C87-081037". Inexplicably, throughout the prosecution of four applications dating from 1989, neither the examiner nor appellants have relied upon the Japanese Patent Publication that forms the basis for the abstract. This is even more puzzling since appellants have submitted the Japanese Patent Publication and a translation thereof in the Information Disclosure Statement filed March 18, 1996 (see Paper No. 40). The examiner initialled Form PTO-1449 and sent the Letter of May 15, 1996 (Paper No. 41) but did not elect to mention the Japanese reference or translation. For purposes of this appeal, we will refer to the translation of Japanese 62-122671 as "Yamamoto" and the Derwent Abstract as the "Abstract".

[4] It is noted that the examiner made new grounds of rejection in the answer. However, in response to appellants' reply brief, the examiner has withdrawn all new grounds of rejection (see the Supplemental Examiner's Answer mailed Sept. 13, 1996). These rejections are therefore not before us on appeal.

*OPINION*

The physiological visco-elastic formulation of appealed claim 1 contains 0.1 to about 5% hyaluronate salt in a balanced salt solution containing 2.6 to 3.9 millimoles (mM) of calcium ions and 1.2 to 1.8 mM of magnesium ions, with the formulation being free of phosphates.

The Abstract discloses a formulation of 1 to 2% hyaluronate and/or hydroxypropylmethyl cellulose (HPMC) in a balanced salt solution containing calcium and magnesium ions. The formulation is free of phosphates and useful for preventing corneal damage in eye operations. Similarly to appellants' formulation, the Abstract teaches that the preferred buffer is one whose composition resembles that of the aqueous humor. The Abstract discloses one specific example to a balanced salt solution containing magnesium ions and calcium ions with HPMC.

Appellants cite Gasser in the brief (page 6) as prior art that shows the composition of the human aqueous humor is well known[5]. Gasser also discloses the relatively similar BSS and

[5] "Effects of Intraocular Irrigating Solutions on the Corneal Endothelium After in Vivo Anterior Chamber

BSS PLUS physiologic irrigation solutions for use during surgical procedures of the eye (BSS is discussed on page 5 of the specification).

The examiner's position is that the Abstract teaches magnesium salt as one of many ingredients in a hyaluronate (and/or HPMC) solution (answer, pages 2-3). The examiner further states that every claimed salt component is disclosed by the Abstract and "[T]o modify the concentrations of the prior art composition and use it for the same purpose would have been within the skill of [the] artisan" (answer, page 3).

Appellants argue that the Abstract fails to establish a *prima facie* case of obviousness for the following reasons: (1) no magnesium is present in the preferred buffer solution of the Abstract; (2) no hyaluronate salt is present in the single example of the Abstract; (3) even when magnesium is included in the Abstract, it occurs at a much higher concentration than that of the appealed claims; and (4) the purpose of the

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Irrigation", Gasser et al., Am. J. Ophthalmology 99:321-328, March 1985 (only page 322 of record).

magnesium is different in the Abstract than in the present application (see the brief, pages 5-7 and 9-10).

It is clear from Yamamoto that magnesium and calcium ions are present in buffered solution with hyaluronate salt (see the second example of the translation at page 6). This "Embodiment 2" of Yamamoto rebuts appellants' first two arguments. Regarding the argument that the concentration of the magnesium taught by Yamamoto was higher than appellants' claimed concentrations[6], it would have been well within the skill of the art to modify the concentrations disclosed by Yamamoto in light of the teaching by Yamamoto that "[A]djustment is desired so that it has a liquid characteristic resembling the nature and concentration existent within the aqueous humor within the eye" (page 3). Given the well known composition and concentrations in the aqueous humor of the human eye (see Gasser), it would be

[6] Appellants present the differing concentrations on page 6 of the brief without explanation as to how the mM concentration of Mg was calculated for the Abstract. From our calculations, the Mg concentration of the Abstract is 2.5 mM (1 mole $MgSO_4$/120.3 g X 1000 ml/1 liter X 0.03 g $MgSO_4$/100 ml of solution). However, since this value is similar to appellants' calculated value of 2.63, for purposes of this appeal we will use appellants' value.

routine experimentation to determine the optimum concentrations of each component of the formulation of Yamamoto. The concentrations would not have to be exactly the same as in the aqueous humor of the human eye (note the differing concentrations of the components for BSS and BSS PLUS). Appellants have failed to note that the concentration of the other important ion (calcium) disclosed by the Abstract is very similar to the aqueous humor of the human eye (1.82 mM of calcium in the Abstract vs. 1.8 mM from Gasser) but the concentration of calcium in the appealed claims is much higher (2.6 to 3.9 mM, see claim 1).

As to appellants' final argument, we can find no support in the Abstract or Yamamoto for appellants' allegation that magnesium is only present in the reference as a counter or carrier ion for sulfate. It appears, since sulfate is not listed as a constituent of the human aqueous humor (see Gasser), that magnesium is the important ion and that sulfate is only used as a counter or carrier ion.

The Abstract and Yamamoto disclose every aspect of the claimed subject matter except the specific concentrations. These concentrations, as noted above, would be well within the

ordinary skill of the art given the teaching of the Abstract and Yamamoto that the formulation should resemble the well known nature and concentration existing within the aqueous humor of the human eye.

For the foregoing reasons, we conclude that the subject matter of claims 1 to 20 would have been *prima facie* obvious based on the disclosure and teachings of the Abstract and Yamamoto. The burden of coming forward with evidence or argument shifts to the appellants. After evidence or argument is submitted by the appellants in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

Appellants submit that the Mello Declaration under 37 CFR § 1.132, filed Dec. 14, 1992, shows that the present hyaluronate-containing compositions provide unexpected benefits (brief, pages 3-5). The Mello Declaration identifies an abstract of a McCulley et al. article (hereafter "McCulley") that compares Vitrax, a commercial embodiment of

the present invention, with Amvisc and Healon, two commercially available hyaluronate-containing compositions that include no magnesium ions.

The examiner notes that the comparison in the Declaration is with compositions that contain no magnesium ions but the prior art used in the rejection "clearly contains magnesium" (answer, pages 5-6). The examiner further states that "[A]ppellant has presented no evidence to establish the criticality of the concentrations used by the present application over the prior art of record" (answer, page 6).

A Rule 132 affidavit (or declaration), to be effective, must compare the claimed subject matter with the closest prior art. *In re Burckel*, 592 F.2d 1175, 1179, 201 USPQ 67, 71 (CCPA 1979). We agree with the examiner that the Amvisc and Healon compositions, which do not contain "significant concentrations" of calcium or magnesium ions (see page 2 of the Mello Declaration), are not the closest prior art. Yamamoto contains magnesium and calcium ions in similar concentrations and is the closest prior art of record. Furthermore, it is not clear if the claimed subject matter was

compared. The McCulley article compares Vitrax (E. Weck), Amvisc, Healon and two laboratory formulations using the same concentration of Vitrax SH (sodium hyaluronate). Neither McCulley nor the declarant Mello identifies these laboratory compositions[7]. However, it appears that the best results occurred with these lab formulations. For the first procedure, the lab formulations were nontoxic while Vitrax caused some transient acute damage (although it was much less toxic than Amvisc or Healon). For the second procedure (to simulate leaving the material in place after surgical closure), all of the commercial preparations (Vitrax, Amvisc, and Healon) were toxic. The McCulley article further states that the lab formulations using Weck SH were tolerated longer than any of the commercial products. To properly evaluate the comparisons in the McCulley article, the compositions of each preparation would have to be known to determine if the claimed subject matter was compared against the closest prior art.

[7] Mello does identify the Vitrax formulation as being "substantially identical" to the ionic composition of appealed claim 9 (Declaration, page 1). VITRAX™ is identified by a product information sheet , filed on Oct. 1, 1993,as Paper No. 30. Neither appellants nor declarant state whether the Vitrax (E. Weck) of the McCulley article is equivalent to VITRAX™.

For the foregoing reasons, we conclude that the subject matter of claims 1 to 20 would have been *prima facie* obvious based on the disclosure and teachings found in the Abstract and Yamamoto. We also conclude that appellants have not presented objective evidence of nonobviousness, on this record, which would serve to rebut the *prima facie* case. Accordingly, the examiner's rejection of claims 1 to 20 under 35 U.S.C. § 103 as unpatentable over the Abstract is affirmed. However, since we have elaborated on the reasoning of the examiner and referred to the translation of the Japanese reference and Gasser that was the basis of the abstract, we denominate this "affirmance" as a new ground of rejection pursuant to our authority under 37 CFR § 1.196(b).

Any request for reconsideration or modification of this decision by the Board of Patent Appeals and Interferences based upon the same record must be filed within one month from the date of the decision. 37 CFR § 1.197. Should appellants elect to have further prosecution before the examiner in response to the new rejection under 37 CFR § 1.196(b) by way of amendment or showing of facts, or both, not previously of

record, a shortened statutory period for making such response is hereby set to expire two months from the date of this decision.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

*AFFIRMED - 37 CFR § 1.196(b)*

RICHARD E. SCHAFER )
Vice Chief Administrative Patent Judge )
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) BOARD OF PATENT
JOHN D. SMITH ) APPEALS AND
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Appeal No. 95-2655
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